

## **II. REMARKS**

### **A. Status of the Claims**

Claims 1, 7-14, 17-18, 20-21, 24-31, 35, and 39-47 were pending in the case at the time of the Office Action. Claims 1, 14, and 31 have been amended in the Amendment set forth herein. New claims 48 and 49 are added, and no additional claims are canceled. Claims 2-8, 15-16, 19, 22-23, 32-34, and 36-38 are canceled without prejudice or disclaimer. Therefore, claims 1, 9-14, 17-18, 20-21, 24-31, 35, and 39-49 are currently under consideration.

Applicant reserves the right to prosecute the subject matter of any canceled claims or the subject matter omitted from any of the originally filed claims in a continuation or divisional application.

Regarding the amendment to claims 1, 14, and 31, these claims have been amended to recite the phrase “wherein an engraftment factor selected from the group consisting of G-CSF, IL-1, VEGF, Flt-3 ligand, Akt, hemeoxygenase, nitric oxide, 5-azacytidine, collagen, laminin, and fibronectin is administered to the human subject concurrently with or following the implanting of the population of isolated stem cells in an amount and for a time sufficient to promote engraftment of the cells in the subject, ...” Support for this limitation can be found generally throughout the specification, such as in originally filed claims 7, 8, 24, 25, 39, and 40. Support for the new claims can be found generally throughout the specification, such as on page 20, lines 1-17 (claim 48), and original claims 7, 8, 24, 25, 39, and 40 (claim 49).

### **B. The Rejections Under 35 U.S.C. §103(a) Are Overcome**

#### **1. Rejections Based on Kocher and Kalka In View of Gillis**

Claims 1, 7-14, 17, 18, 20, 21, 24-31, 35, 39-45, and 46 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kocher and Kalka in view of U.S. Patent 5,199,942 (“Gillis”). Applicant respectfully traverses.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (3) there must be a reasonable expectation of success. *Manual of Patent Examining Procedure* § 2142. See also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991). All three elements must be shown to establish a *prima facie* case of obviousness. Thus, if one element is missing, a *prima facie* case of obviousness does not exist.

***a. Kocher, Kalka, and Gillis Fail to Teach or Suggest Each Limitation of the Claimed Invention***

There is no *prima facie* case of obviousness because Kocher and Kalka in view of Gillis does not teach or suggest each limitation of the claimed invention. The Examiner has not cited, nor do Applicants identify, any teaching or suggestion in these references pertaining to administration of an engraftment factor selected from the group consisting of G-CSF, IL-1, VEGF, Flt-3 ligand, Akt, hemeoxygenase, nitric oxide, 5-azacytidine, collagen, laminin, and fibronectin.

There is additionally no *prima facie* case of obviousness because none of the cited references appear to teach the limitation of “a donor who is HLA-matched to the subject and genetically non-identical to the subject.” Gillis pertains to autologous hematopoietic cell transplantation, and not allogeneic transplantation. See entire document, including abstract and field of the invention (col. 1, lines 12-25). Applicants invite the Examiner to identify any such teaching or suggestion in the cited combination of references.

Further, none of the cited references teach or suggest “producing a graft comprising muscle cells.” The Examiner cites to Fig. 2e of Kocher as allegedly teaching this limitation.

However, this figure legend, which recites “endothelial cells lining numerous capillaries (arrows) within myocardial infarct bed,” does not teach or suggest the development of *muscle cells*. Further, the sections of Kalka cited by the Examiner which allegedly teach this limitation do not pertain to the development of muscle cells but address neovascularization. Gillis is not cited as teaching or suggesting this limitation; nor does Applicant identify any such information in Gillis.

***b. The Examiner Has Not Met Her Burden in Setting forth an Analysis Supporting an Obviousness Rejection***

The Examiner argues that the claim term “a graft comprising muscle cells in the damaged or diseased” tissue is “rather vague and broad as claimed and as disclosed.” Applicants first note that this observation appears misplaced in the context of an obviousness rejection in view of the standard for obviousness as discussed above.

The Examiner further appears to argue that Applicants, in order to include a claim to a “graft comprising muscle cells,” must present histological analysis of such a graft. Such a standard for setting forth an obviousness rejection is not consistent with the requirement set forth in case law. In *KSR Int’l Co. v. Teleflex, Inc.*, No. 04-1350 (U.S., Apr. 30, 2007), the Supreme Court noted that the analysis supporting a rejection under 35 U.S.C. §103(a) should be made explicit, and that it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements” in the manner claimed. *KSR*, slip op. at 14. More particularly, the Court noted that “[o]ften, it will be necessary ... to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an *apparent reason* to combine the known elements in the fashion claimed by the patent at issue,” and that “[t]o facilitate review, this analysis *should be made explicit*.” *Id.*, (emphasis added). No such explicit analysis has been set forth by the Examiner. Here, the Examiner has not set forth any basis to

establish that the references which she cites include muscle cells in the graft. Therefore, the Examiner has failed to meet her burden in setting forth this rejection.

Therefore, because the Examiner has failed to set forth a *prima facie* case of obviousness under 35 U.S.C. §103(a), it is respectfully requested that the rejection of claims 1, 7-14, 17, 18, 20, 21, 24-31, 35, 39-45, and 46 should be withdrawn.

**c. *Kocher and Kalka in View of Gillis Fails to Provide Any Suggestion or Motivation to One of Ordinary Skill in the Art to Practice the Claimed Invention***

There is further no *prima facie* case of obviousness because Kocher and Kalka in view of Gillis fails to provide any suggestion or motivation to one of ordinary skill in the art to practice the claimed invention. As discussed above, none of the cited references pertain to production of a graft comprising muscle cells. Further, the claims as presently set forth pertain to allogeneic transplantation from a donor into a human subject. Neither Kocher nor Kalka teach or suggest this limitation. Further, Gillis provides no motivation to provide for this missing information because it pertains to autologous transplantation, and not allogeneic transplantation. Further, as discussed above, none of the cited references teach or suggest the administration of engraftment factors as discussed in the claims.

**d. *The New Claims are Not Rendered Obvious***

New claims 48 and 48 are not rendered obvious by Kocher and Kalka in view of Gillis for the reasons discussed above. Each of these new claims depends from claim 1, which for the reasons discussed above is not rendered obvious. None of the methods of administration recited in claim 48 are taught or suggested by these references, nor are any of the engraftment factors recited in claim 49 taught or suggested by these references. Therefore, the new claims are not unpatentable under 35 U.S.C. §103(a) in view of Kocher, Kalka, and Gillis.

***e. Conclusion***

In view of the above, the Examiner has failed to set forth a *prima facie* case of obviousness based on Kocher in view of Kalka and Gillis. Therefore, it is respectfully requested that this rejection should be withdrawn.

**2. Rejections Based on Pittenger and Fernandez In View of Orlic**

Claims 1, 7-14, 17, 18, 20, 21, 24-31, 35, 39-45, and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,387,369 ("Pittenger") and U.S. Patent 6,261,549 ("Fernandez") taken with Orlic *et al.* (Nature, 2001, Vol. 410, pp. 701-705; "Orlic - 1") or Orlic *et al.* (Blood 2001, Vol. 98, No. 11, part 1, page 810a; "Orlic-2"). Applicant respectfully traverses.

***a. Pittenger and Fernandez in View of Orlic-1 and Orlic-2 Fail to Teach or Suggest Each Limitation of the Claimed Invention***

There is no *prima facie* case of obviousness because Pittenger and Fernandez in view of the Orlic references does not teach or suggest each limitation of the claimed invention.

There is no *prima facie* case of obviousness because these references do not teach or suggest each limitation of the claimed invention. The Examiner has not cited, nor do Applicants identify, any teaching or suggestion in these references pertaining to administration of an engraftment factor selected from the group consisting of G-CSF, Il-1, VEGF, Flt-3 ligand, Akt, hemeoxygenase, nitric oxide, 5-azacytidine, collagen, laminin, and fibronectin.

Further, none of the cited references teach the limitation of "a donor who is HLA-matched to the subject and genetically non-identical to the subject," a limitation which is present in each of the pending claims. Fernandez appears silent as to the HLA status of the donor. Pittenger discloses that the stem cells used in its methods are "preferably autologous" rather than genetically non-identical. See col. 1, lines 45-48. Neither of the Orlic references appear to address HLA-matching of the subjects. Applicants invite the Examiner to identify any such

teaching or suggestion in the cited combination of references. Furthermore, none of the cited references teach or suggest any of the mobilization factors set forth in any of claims 1, 14, and 31.

**b.      *The New Claims are Not Rendered Obvious***

Regarding new claims 46 and 47, there is no *prima facie* case of obviousness for the reasons discussed above, as these claims depend from claim 1. None of the methods of administration recited in claim 48 are taught or suggested by these references, nor are any of the engraftment factors recited in claim 49 taught or suggested by these references. Therefore, the new claims are not unpatentable under 35 U.S.C. §103(a) in view of Pittenger, Fernandez, or the Orlic references.

**c.      *Conclusion***

In view of the above, there is no *prima facie* case of obviousness as to each of the cited claims. Therefore, it is respectfully requested that this rejection should be withdrawn.

**C.      *Conclusion***

In view of the foregoing, each of the pending claims is in condition for allowance, and a Notice of Allowance is earnestly solicited. The Examiner is invited to contact the undersigned attorney at 512.536.5639 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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